REMARKS

Claims pending herein are directed to methods that include determining the presence or absence of a polymorphic variation associated with breast cancer in a specific region of the human genome. The claims specify the one or more polymorphic variations are in a region between about chromosome position 117925391 and about chromosome position 117945870 according to Build 31 of the GenBank database human genome sequence.

The Office rejected the pending claims for alleged lack of enablement and alleged lack of written description under 35 U.S.C. 112, first paragraph. In response to these rejections, Applicant files herewith a declaration by Dr. Charles Cantor under 37 C.F.R. 1.132 (the "Cantor Declaration"). The Cantor Decarlation shows the named inventors had possession of the claimed subject matter at the time the above-identified patent application was filed, and provides further evidence that the specification enables the pending claims.

The Cantor Declaration addresses methodology performed by the named inventors that resulted in the claimed subject matter. The Cantor Declaration concludes the named inventors determined the region claimed was significantly associated with breast cancer by (i) identifying a locus containing an incident polymorphic marker associated with the disease in a genome-wide scan, and (ii) verifying multiple polymorphic sites proximal to the incident marker in the locus also were associated with the disease (Cantor Declaration, paragraph 3).

The Cantor Declaration also shows the methodology and results obtained by the named inventors are supported by accepted genetic principles (Cantor Declaration, paragraph 4). In particular, the declaration states the named inventors identified the claimed region as being associated with breast cancer when they verified multiple polymorphic variants in the region were significantly associated with the disease.

The Cantor Declaration shows that other research groups using similar methodology have successfully identified another disease-associated region in the human genome (Cantor Declaration, paragraph 5). Accordingly, the

methodolgy has been independently and successfully utilized after the filing date of the patent application herein to identify disease-associated regions.

That the named inventors identified the disease-associated region claimed by analyzing a representative number of polymorphisms also is described in the Cantor Declaration. Paragraph 6 of the Cantor Declaration shows that the named inventors analyzed 42% of the polymorphisms currently in the HapMap database having a minor allele frequency of greater than 0.05 in the claimed sub-region. This analysis compares the number of polymorphisms in the claimed region presently in the HapMap database to the number of polymorphisms described in the patent application more than three-and-a-half years ago, and therefore, the degree of overlap described in the Cantor Declaration likely is under estimated. The Cantor Declaration also states this degree of overlap is on par with, or better than, the degree of overlap others had when making disease associations after the above-identified patent application was filed.

In paragraph 7, the Cantor Declaration outlines experimental evidence in the specification that supports the named inventors' determination the claimed region was associated with breast cancer. This evidence in the specification was addressed previously in the amendment and response filed on May 18, 2007.

Application of the Cantor Declaration to Outstanding Rejections

The Office stated in the interview summary dated April 26, 2007 that guidance in the specification did not allow the skilled artisan to determine which of the polymorphisms, identified after the invention was filed, were and were not associated with the disease. The Office also stated in the interview summary that trial and error experimentation would be required to identify which of the additional polymorphisms were disease associated.

The Cantor Declaration shows this rationale is not applicable to the subject matter currently claimed. The claimed processes include determining the presence or absence of a polymorphic variation associated with breast cancer in the sub-region specified. The Cantor Declaration shows the named inventors identified this sub-region is associated with breast cancer, and provided a

representative number of polymorphic variations associated with breast cancer in the sub-region. Accordingly, evidence in the Cantor Declaration shows the named inventors had possession of the claimed subject matter at the time the patent application was filed in accordance with the written description requirement of 35 U.S.C. 112, first paragraph.

Disclosure of the claimed "hot zone" in the specification also enables the claimed subject matter. In particular, disclosure of the sub-region claimed, or "hot zone," guides the person of ordinary skill in the art to a region associated with breast cancer. Armed with this information, the person of ordinary skill in the art could readily determine whether there are any polymorphic variations associated with breast cancer in the claimed sub-region other than those described in the specification. Because the specification describes a number of methods for typing polymorphic variants known in the art at the time of filing, as addressed in previous submissions by Applicant, such a determination would be routine. In support of the routine nature of such studies, please refer to Applicant's discussion of the specification's enabling disclosure in view of the *In re Wands* decision, presented previously. Thus, the specification meets the requirements for enablement under 35 U.S.C. 112, first paragraph.

Accordingly, the specification enables and provides a written description of the claimed subject matter, as evidenced by the Cantor Declaration. Applicant therefore respectfully requests withdrawal of the outstanding rejections under 35 U.S.C. 112, first paragraph.

CONCLUSIONS

Applicant respectfully submits all pending claims will be in condition for allowance upon entry of the amendments herein. Applicant respectfully solicits a prompt notification to this effect, and the Examiner is encouraged to contact the undersigned representative (contact information below) to promptly resolve any remaining issues or questions.

In the unlikely event a fee calculation document or other pertinent document is separated from this submission and the Office determines that an extension and/or other relief is required, Applicant petitions for any required relief, including extensions of time, and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. **50-3473**.

Respectfully submitted,

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